

Appl. No. 09/929,863  
Amdt. Dated August 21, 2003  
Reply to Office action of March 12, 2003

### IN THE CLAIMS:

Claim 1. (Currently amended) A method to induce differentiation of ~~a~~ an isolated or purified naïve CD4<sup>+</sup> T cell to a Tr1 cell comprising contacting the naïve CD4<sup>+</sup> T cell with an appropriate amount of interferon- $\alpha$  (IFN- $\alpha$ ) and an appropriate amount of IL-10.

Claim 2. (Currently amended) The method of Claim 1, wherein said Tr1 cell is characterized by:

- a) CD4 expression;
- b) high levels of IL-10 production;
- c) significant levels of TGF- $\beta$  or IFN- $\gamma$  production; and
- d) little or no production of IL-4 or IL-2.

Claim 3. (Currently amended) The method of Claim 2, wherein:

- a) ~~said high level of the~~ IL-10 production is at least 6000 pg in 1 ml for ~~10<sup>6</sup> cells~~ in 48 h;
- b) ~~said significant level of the~~ TGF- $\beta$  production is at least 600 100 pg in 1 ml for ~~10<sup>6</sup> cells in 48 h;~~
- c) ~~said significant level of the~~ IFN- $\gamma$  production is at least 4000 400 pg in 1 ml for ~~10<sup>6</sup> cells in 48 h;~~
- d) ~~said little or no the~~ IL-4 production is less than 200 pg in 1 ml for ~~10<sup>6</sup> cell in~~ 48 h; or
- e) ~~said little or no the~~ IL-2 production is less than 200 pg in 1 ml for ~~10<sup>6</sup> cell in~~ 48 h;

when evaluated from cultures of about 10<sup>6</sup> cells per ml per 48 hours.

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Claim 4. (Currently amended) The method of Claim 2, wherein:

- a) ~~said high level of the~~ IL-10 production is at least ~~6000~~ 12000 pg in 1 ml for ~~10<sup>6</sup> cells in 48 h;~~
- b) ~~said significant level of the~~ TGF- $\beta$  production is at least 600 pg in 1 ml for ~~10<sup>6</sup> cells in 48 h;~~
- c) ~~said significant level of the~~ IFN- $\gamma$  production is at least 1000 pg in 1 ml for ~~10<sup>6</sup> cells in 48 h;~~
- d) ~~said little or no the~~ IL-4 production is less than ~~200~~ 100 pg in 1 ml for ~~10<sup>6</sup> cell~~ in 48 h; or
- e) ~~said little or no the~~ IL-2 production is less than ~~200~~ 100 pg in 1 ml for ~~10<sup>6</sup> cell~~ in 48 h;

when evaluated from cultures of about 10<sup>6</sup> cells per ml per 48 hours.

Claim 5. (Original) The method of Claim 2, wherein said Tr1 cell:

- a) has a reduced proliferative potential in response to polyclonal activation;  
and/or
- b) suppresses response to alloantigens by responder T cells.

Claim 6. (Currently amended) The method of Claim 1, wherein said Tr1 cells cell suppresses antigen-specific activation of a naive autologous T cells cell.

Claim 7. (Original) The method of Claim 5, wherein said suppressed response to alloantigens is mediated by IL-10 and/or TGF- $\beta$ .

Claims 8-10. (Cancelled).

Claim 11. (Original) The method of Claim 1, wherein said contacting is in combination with an antigen.

Claim 12. (Original) The method of Claim 11, wherein said antigen is an alloantigen.

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Claim 13. (Currently amended) The method of Claim 1, wherein said Tr1 ~~cells are~~ cell  
is further proliferated in IL-15.

Claim 14. (Currently amended) The method of Claim 1, wherein said Tr1 ~~cells are~~ cell  
is further tested for antigen specificity.

Claims 15-18. (Cancelled).

Claim 19. (New) A method to induce differentiation of an isolated or purified cord blood  
T cell to a Tr1 cell comprising contacting the cord blood cell with an appropriate amount  
of IFN- $\alpha$ .